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## Differences in biomarkers and molecular pathways according to age for patients with HFrEF

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**Breast cancer**

- Signaling by NOTCH1
- Autocyte differentiation
- GRN
- NOTCH1 Activation and Transcription of Signal to the Nucleus
- MBL1
- NOTCH1
- OLL1
- RNG8

**Bladder cancer**

- Pancreatic cancer
- Prostate cancer
- Non-small cell lung cancer
- Endometrial cancer
- Melanoma
- Adhesion junction
- Interleukin-4 and Interleukin-13 signaling
- Central carbon metabolism in cancer

**Proteoglycans in cancer**

- GSK3B
- CDK1A
- RAS

**Cytokine-cytokine receptor interaction**

- TNF signaling
- IL-6
- TNFRSF10B
- TNFRSF10A
- TNFRSF10C
- TNFRSF10D
- TNFRSF10E
- TNFRSF10F
- TNFRSF10G
- TNFRSF10H
- TNFRSF10I
- TNFRSF10J
- TNFRSF10K
- TNFRSF10L
- TNFRSF10M
- TNFRSF10N
- TNFRSF10O
- TNFRSF10P
- TNFRSF10Q
- TNFRSF10R
- TNFRSF10S
- TNFRSF10T
- TNFRSF10U
- TNFRSF10V
- TNFRSF10W
- TNFRSF10X
- TNFRSF10Y
- TNFRSF10Z

**Response to hypoxia**

- HIF-1α pathway
- EPO

**AGE-RAGE signaling pathway in diabetic complications**

- RAGE
- Sema3
- AGEs

**Taste receptor activity**

- TAS2R family

**Regulation of bone resorption**

- TNF signaling
- osteoclasts

**Signaling by PDGF**

- PDGFR
- PI3K/Akt

**Regulation of insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs)**

- IGF
- IGFBP

**Positive regulation of osteoblast proliferation**

- BMP signaling

**Degradation of the extracellular matrix**

- MMPs
- collagen

**Extracellular matrix organization**

- ECM components

**Virus receptor activity**

- GPCRs
- viral receptors

**Negative regulation of response to wounding**

- wound healing factors

**Negative regulation of blood coagulation**

- coagulation cascade

**Complement and coagulation cascades**

- complement system

**Glycosaminoglycan catabolic process**

- glycosaminoglycans

**ECM proteoglycans**

- proteoglycans

**Non-integrin membrane-ECM interactions**

- integrins
- cadherins

**Integrin cell surface interactions**

- integrins
- focal adhesion

**Endothelial cell differentiation**

- endothelial cells

**Elastic fiber formation**

- elastic fibers

**Collagen degradation**

- collagenase

**Collagen organization**

- collagen

[illegible]

Figure 2 is a bar chart with a secondary y-axis. The left y-axis represents the 'Number of genes involved' on a logarithmic scale from 1 to 1000. The right y-axis represents the '-log(false discovery rate)' on a linear scale from 0 to 5. The x-axis lists 15 biological processes. The legend indicates three data series: 'Observed gene count' (blue bars), '-log(false discovery rate)' (orange line with dots), and 'Background gene count' (green bars). The observed gene count is consistently lower than the background gene count for all processes. The -log(false discovery rate) is highest for 'Cytokine-cytokine receptor interaction' and decreases as the number of genes involved decreases.

Biological Process	Observed gene count	Background gene count	-log(false discovery rate)
Cytokine-cytokine receptor interaction	~80	~1800	~4.5
Proteoglycans in cancer	~60	~1500	~3.5
MAPK signaling pathway	~50	~1400	~3.0
PI3K-Akt signaling pathway	~50	~1500	~3.0
MicroRNAs in cancer	~40	~1300	~3.0
EGFR tyrosine kinase inhibitor resistance	~30	~1100	~2.5
Endocrine resistance	~30	~1100	~2.5
ErbB signaling pathway	~30	~1100	~2.5
HIF-1 signaling pathway	~30	~1100	~2.5
TGF-beta signaling pathway	~30	~1100	~2.5
Adherens junction	~30	~1000	~2.5
Th17 cell differentiation	~30	~1100	~2.5
Pathways in cancer	~50	~1800	~2.5
Pancreatic cancer	~30	~1000	~2.5